Impurity profiling/comparative analyses of samples of 1-phenyl-2-propanone

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ABSTRACT

1-Phenyl-2-propanone (P-2-P), also known as benzyl methyl ketone (BMK), is the main precursor used in amphetamine synthesis. In recent years, the number of seizures of P-2-P from both licit and illicit drug manufacture has increased. The present article comprises a discussion of some of the largest seizures of P-2-P diverted from regular production to the illicit market. It also presents the methods used in clandestine laboratories to synthesize P-2-P and a forensic approach to identify and differentiate between these methods.

To that end, and to facilitate the monitoring of the P-2-P market, a method of P-2-P impurity profiling was designed for comparative purposes and for the identification of the synthesis route. P-2-P samples were analysed by means of gas chromatography/mass spectrometry (GC/MS). Out of 36 identified impurities, 14 were selected as markers for sample comparison. On the basis of the GC peak areas of those 14 markers, a cluster analysis was carried out, resulting in three clusters, each corresponding to a given P-2-P synthesis route.

The results of P-2-P impurity profiling are stored in both a forensic database and a police database. The forensic database comprises chemical data, such as those on P-2-P purity, additives and specific impurities, as well as information on seized P-2-P samples having a similar impurity profile. Data stored in the police database, which is linked with the forensic database by case identification number, cover the circumstances of seizures and personal details of offenders. The databases enable the full use of forensic data in intelligence work and police investigative activities.

Keywords: 1-phenyl-2-propanone; profiling; cluster analysis; synthetic methods; mass spectrum; intelligence; law enforcement; clandestine laboratories

Introduction

Poland, together with Belgium and the Netherlands, is one of the main countries in which amphetamine is manufactured for the illicit market. In Poland, several

clandestine laboratories manufacturing amphetamine by means of Leuckart synthesis are closed down every year. In order to suppress this branch of illicit drug manufacture, law enforcement authorities strive to reach illicit producers and "retailers" of the main precursor: 1-phenyl-2-propanone (P-2-P), also known as benzyl methyl ketone (BMK).

In the last several years, there have been several seizures of P-2-P and dismantlings of clandestine P-2-P laboratories in Poland. The appearance on the illicit market of P-2-P originating from both legitimate (through diversion) and illicit manufacture called for the development of an analytical method that would make it possible to differentiate production batches of precursors. Furthermore, the police demanded answers to questions such as which P-2-P samples might come from the same source and what their method of synthesis was.

In order to meet those expectations, a method of P-2-P impurity profiling was elaborated. The main purpose of the method is to assist the police in their efforts to combat the illicit manufacture of and trafficking in P-2-P. The identification of the synthesis method allows the police to focus their site investigations on specific chemicals, while the identification of links between P-2-P samples facilitates the monitoring of trafficking in that precursor, as well as the identification of the sources and smuggling routes used.

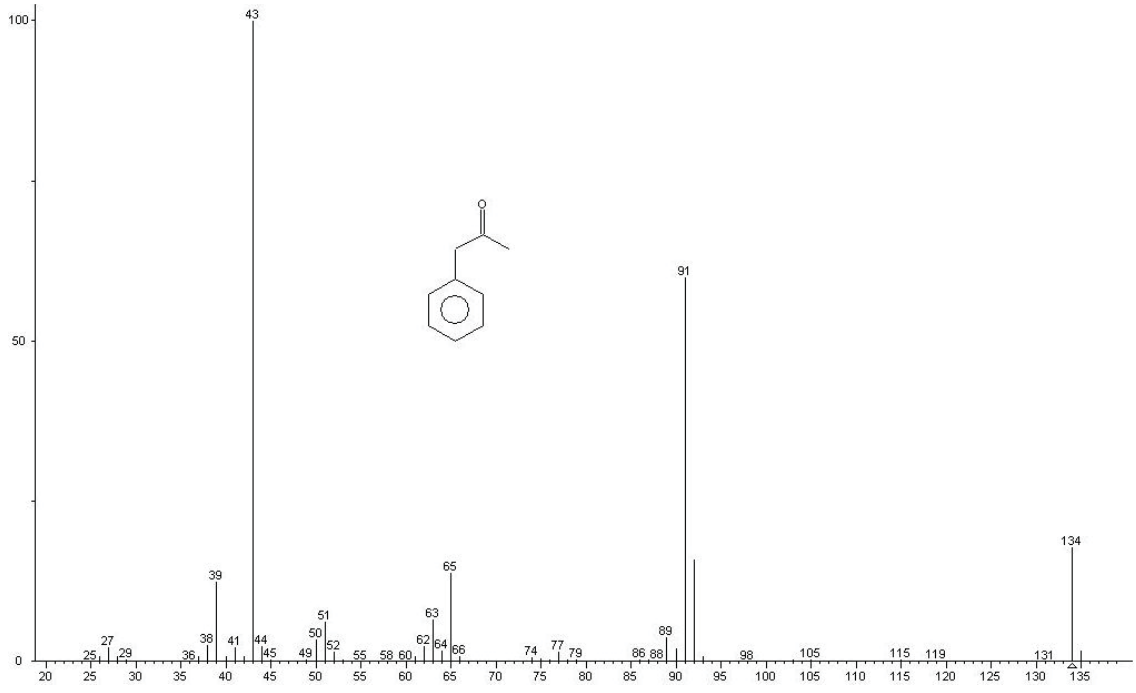
1-Phenyl-2-propanone

Characteristics of 1-phenyl-2-propanone

P-2-P is a colourless or slightly yellowish liquid. The colour of illicitly manufactured P-2-P may vary from yellow to dark brown. It has a density similar to that of water and a pleasant scent. P-2-P is most frequently used as a precursor for the manufacture of amphetamine. The mass spectrum and molecular formula of P-2-P are shown in figure I; physical and chemical data for P-2-P are as follows:

Name used in Table I of the 1988 Convention:	1-phenyl-2-propanone
Other names:	P-2-P; benzyl methyl ketone (BMK); phenylacetone
Chemical Abstracts Service number:	103-79-7
Molar mass:	134.18
Molecular formula:	$C_9H_{10}O$
Melting point:	−15 °C
Boiling point:	214 °C
Density:	1.0157 g/cm^3

Figure I. Mass spectrum and molecular formula of 1-phenyl-2-propanone



Manufacture and legitimate and illegal uses

At the moment, countries where P-2-P is licitly manufactured are difficult to name because relevant data vary, depending on the source of the data. For example, the European Anti-Fraud Office (OLAF) mentions China, France and Japan among licit producers, while the International Narcotics Control Board (INCB) would also add India and the United States of America to the list. Up-to-date information on the total annual volume of world P-2-P manufacture is still unavailable.

Despite the lack of official data, the analysis of the situation in the area of illicit manufacture of synthetic drugs allows speculation that licit manufacture of P-2-P takes place also in the Russian Federation and Ukraine.

The legitimate use of P-2-P in the chemical and pharmaceutical industries is practically limited to the manufacture of amphetamine and methamphetamine and their derivatives. Another legitimate use of P-2-P is to produce, through photolysis, benzyl radicals, which in turn are used for the production of propylhexedrine in the process of organic synthesis. In Turkey and the United States, P-2-P is also found in cleaning agents and stain removers. In Poland, P-2-P has no legitimate use other than in scientific research.

In addition, P-2-P is used as a precursor for the illicit manufacture of amphetamine and methamphetamine. It is estimated that P-2-P is used to manufacture nearly 100 per cent of amphetamine from illicit sources and approximately 10 per cent of methamphetamine from illicit sources.

The official price of P-2-P is about €100 per kilogram, while the mean European black market price is approximately €900 per kilogram.

Methods of synthesis of 1-phenyl-2-propanone, with particular emphasis on those employed in clandestine laboratories

P-2-P is a substance listed in Table I of the United Nations Convention against Illicit Trafficking in Narcotic Drugs and Psychotropic Substances of 1988 [1] and, because its legitimate uses are limited, its availability on the licit market is also limited. As a result, one apparent advance has been observed in methods of illicit P-2-P synthesis. Among several dozen known synthesis routes, the ones most frequently encountered in clandestine laboratories are those starting from phenylacetic acid, benzyl cyanide and benzaldehyde (nitrostyrene method).

Synthesis from phenylacetic acid

In recent years, synthesis of P-2-P from phenylacetic acid has become one of the most popular methods used in clandestine laboratories. Although phenylacetic acid is a controlled substance, it is readily available because of its widespread industrial use. In some cases, clandestine laboratories replace the controlled phenylacetic acid with phenylacetic acid chloride, which is subsequently transformed into phenylacetic acid by mixing with water. P-2-P can be generated in a reaction of phenylacetic acid with acetic acid or acetic anhydride, and both acetic acid or acetic anhydride are cheap and easy to procure. Two significant difficulties in the synthesis of P-2-P from phenylacetic acid are the stringent reaction conditions and poor product yield. Despite those drawbacks, illicit manufacture of P-2-P from phenylacetic acid has proved to be cost-effective and constitutes a notable contribution to the illicit precursor market.

Synthesis from phenylacetic acid and acetic acid

Synthesis of P-2-P from phenylacetic and acetic acid is a straightforward, one-step process.

$$\text{Phenylacetic acid} + \text{acetic acid} \rightarrow \text{P-2-P}$$

However, it requires sophisticated equipment, high temperatures and high pressure.

The yield of this reaction is approximately 50 per cent; that is, 500 ml of P-2-P are synthesized from 1 kg of phenylacetic acid.

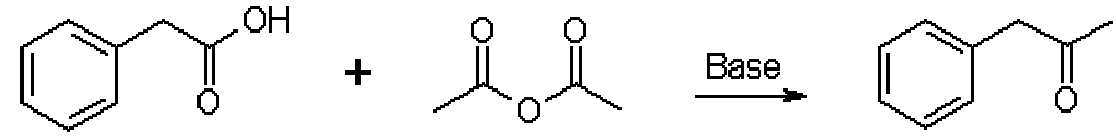
Indicators of synthesis of 1-phenyl-2-propanone from phenylacetic acid and acetic acid

- Phenylacetic acid and acetic acid have a characteristic sharp odour
- Sophisticated equipment and/or stringent reaction conditions:
  - A steel reaction vessel, as well as heating units and equipment used for sustaining temperatures in the range of 300°-400 °C
  - Bottles with nitrogen for regeneration of catalyst
- High consumption of electricity on the premises to sustain high temperatures
- Phenylacetic acid chloride (a non-scheduled substance) can be used instead of phenylacetic acid.

Synthesis from phenylacetic acid and acetic anhydride

Unlike the synthesis route using acetic acid, the reaction of phenylacetic acid with acetic anhydride (see figure II) does not require extreme conditions. The reaction occurs at the boiling point of the reaction mixture, about 150 °C, and requires only basic glassware.

Figure II. Synthesis of 1-phenyl-2-propanone from phenylacetic acid and acetic anhydride



Phenylacetic acid + acetic anhydride ➔ P-2-P

The yield ranges from 50 to 70 per cent; that is 500-700 ml of P-2-P can be obtained from 1 kg of phenylacetic acid.

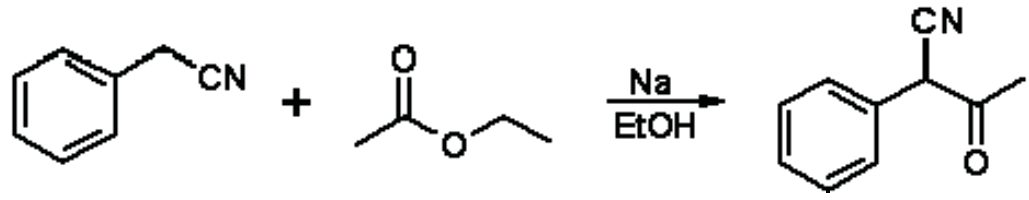
Indicators of synthesis of 1-phenyl-2-propanone from phenylacetic acid and acetic anhydride

- Phenylacetic acid and acetic anhydride have a characteristic sharp odour.
- Considerable amounts of acetic acid salt are required (sodium acetate, potassium acetate or lead acetate).
- During the synthesis, large quantities of carbon dioxide gas are released.

Synthesis from benzyl cyanide

Benzyl cyanide is commonly used in the pharmaceutical industry. It is not classified as a controlled substance under European Parliament and Council Regulation No. 273/2004 and therefore is a precursor of choice among illicit manufacturers of P-2-P. The synthesis of P-2-P from benzyl cyanide occurs in two stages. During the first stage (see figure III) benzyl cyanide is condensed with ethyl acetate in the presence of sodium ethylate.

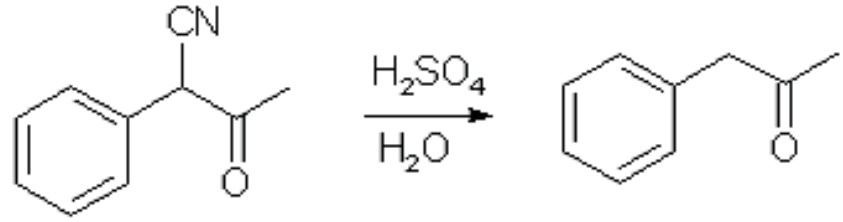
Figure III. Synthesis of 1-phenyl-2-propanone from benzyl cyanide, first stage



Benzyl cyanide + ethyl acetate ➔ α-phenylacetoacetonitrile

The second stage (see figure IV) involves hydrolysis of the nitrile group and subsequent decarboxylation of the resulting acid. The overall yield of P-2-P after both steps amounts to approximately 80 per cent; that is, 900 ml of P-2-P can be obtained from 1 kg of benzyl cyanide.*

Figure IV. Synthesis of 1-phenyl-2-propanone from benzyl cyanide, second stage



α-phenylacetoacetonitrile → P-2-P

Indicators of synthesis of 1-phenyl-2-propanone from benzyl cyanide

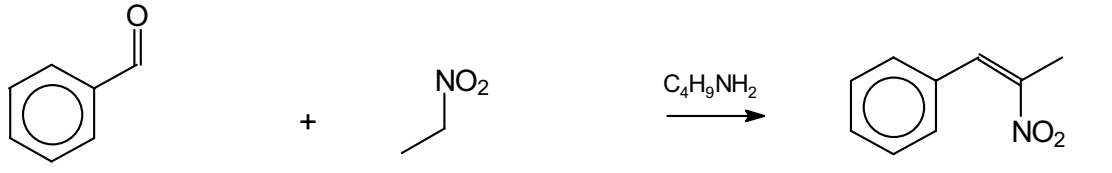
- Metallic sodium used in the first stage ignites upon contact with water (and reacts violently with ethanol), which entails a serious fire risk.
- Phosphoric acid, which has no other application in clandestine laboratories, is used at the stage of hydrolysis and decarboxylation.
- Cooling equipment (ice or dry ice) is vital.
- Due to the need to operate in an anhydrous environment, drying agents, such as calcium oxide or phosphorous pentoxide, are necessary.
- The process has to be conducted by a chemist or a person with vast experience in working in and coping with an anhydrous environment.

*This calculation takes the stoichiometric ratio (i.e. the quantitative relationship) of the molecular masses of the starting material and end product into account.

Synthesis from benzaldehyde

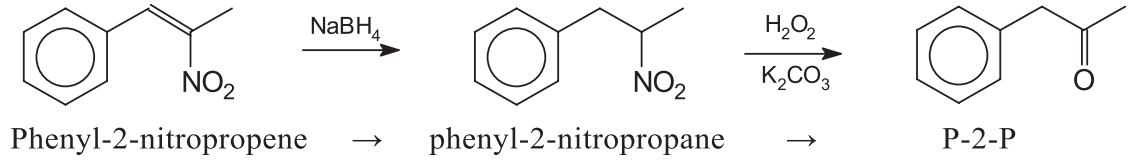
The synthesis of P-2-P from benzaldehyde also occurs in two stages. However, the interval between those stages can be of any desired length, because the intermediate product is chemically stable and can be isolated. In the first stage, an ethanolic solution of benzaldehyde is made to react with nitroethane, using butylamine as a catalyst (see figure V). A crystalline yellow precipitate of phenyl-2-nitropropene is formed at the end of the stage.

Figure V. Synthesis of 1-phenyl-2-propanone from benzaldehyde, first stage: production of phenyl-2-nitropropene



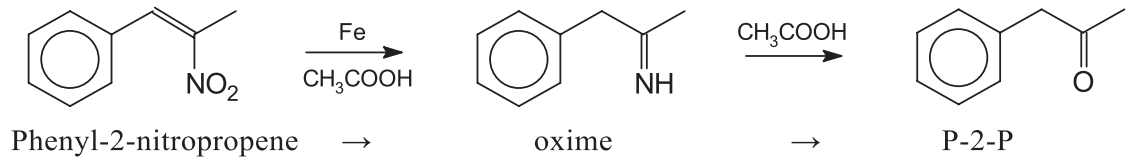
In the second stage of the synthesis, phenyl-2-nitropropene is reduced to phenyl-2-nitropropane, which is subsequently transformed into P-2-P by one of two routes. The first route (see figure VI) results in an overall yield of final product of about 70 per cent; that is, approximately 900 ml of P-2-P are obtained from 1 kg of benzaldehyde.*

Figure VI. Synthesis of 1-phenyl-2-propanone from benzaldehyde, second stage, first route: reduction of phenyl-2-nitropropene to 1-phenyl-2-propanone by means of sodium borohydride



The second route (see figure VII) results in an overall yield of approximately 75 per cent; that is, 960 ml of P-2-P are produced from 1 kg of benzaldehyde.*

Figure VII. Synthesis of 1-phenyl-2-propanone from benzaldehyde, second stage, second route: reduction of phenyl-2-nitropropene to 1-phenyl-2-propanone with ferrous powder in acidic environment



*This calculation takes the stoichiometric ratio (i.e. the quantitative relationship) of the molecular masses of the starting material and end product into account.

Indicators of synthesis of 1-phenyl-2-propanone from benzaldehyde

- Uncommon chemicals, nitroethane and butylamine are used.
- Phenyl-2-nitropropene (intermediate product) is a solid, crystalline substance with a characteristic yellow colour.
- Amphetamine could be produced directly from the intermediate product (phenyl-2-nitropropene), but the use of a strong reducing agent, such as lithium aluminium hydride, would be required.
- Execution of the second stage requires considerable experience on the part of the chemist, and the process must be continuously controlled.

Substantial seizures of 1-phenyl-2-propanone

The International Narcotics Control Board (INCB) reported that in 2001 a total of 23 tons of P-2-P was seized worldwide, the largest total volume ever seized in a single year. The majority of the seizures, totalling 18.2 tons, were effected in the Netherlands, in the port of Rotterdam harbour. The illegal consignments had been shipped from China ([2], paras. 105-106).

Considering the usual modus operandi of criminals on the P-2-P trafficking route leading to the Netherlands (illicit manufacture, or diversion from the legitimate market, in China, followed by smuggling by sea to the Netherlands), the position of Poland is quite interesting. There are reports of P-2-P being smuggled into Poland both by sea from China and overland from the east (Belarus and Ukraine) and the south (Czech Republic). In some years from 1989 to 2000, seizures of P-2-P effected in Poland from land transport were the world's largest: 1.135 tons in 1994 and 710 kg in 1995.

P-2-P seizures in Poland are also associated with detecting, closing down and dismantling clandestine amphetamine laboratories. For example, of the total of 255 kg of P-2-P seized in Poland in 2003, 90 per cent was seized in illicit laboratories raided by the police. According to police investigative findings, in the majority of those cases P-2-P had originated in Belarus or Ukraine.
The following seizures from land transport deserve mention:

(a) On 2 February 1993, at the Medyka border crossing between Poland and Ukraine, 290 l of P-2-P were discovered in a truck driven by a Bulgarian citizen. The precursor was concealed in wood-impregnated barrels. The smuggling route from Bulgaria to Poland led through Romania and Ukraine. The shipment was to be delivered to a Warsaw company specially set up by an organized criminal group in order to facilitate criminal activities. The initial source of the P-2-P shipment from Bulgaria was not identified;

(b) On 14 February 1994, at the Cieszyn border crossing between the Czech Republic and Poland, 700 kg of P-2-P was found hidden in a truck with a Bulgarian registration plate, driven by a Bulgarian citizen. The route from Bulgaria to Poland went through Hungary and the Czech Republic. As in the

previous case, the consignee was a company specifically set up by an organized criminal group and the source of the P-2-P shipment remained unknown;

(c) On 26 December 1994, at the Hrebenne border crossing with Ukraine, 435 l of P-2-P was being smuggled from Ukraine to Poland in the petrol tank of a truck registered in Ukraine and driven by a Ukrainian citizen. Ukraine was identified as the country of origin of the P-2-P consignment;

(d) Two subsequent confiscations of considerable amounts of P-2-P shipped from Belarus (100 l in 2001 and 57 l in 2002) persuaded the criminals to change their smuggling method; the transporting of huge quantities of the precursor was given up. Nowadays, "retail smuggling" predominates, whereby smaller quantities of P-2-P are carried by couriers in, for example, hot water bottles (capacity: 1 l);

(e) The largest attempted illegal import of P-2-P into Poland took place in 2004 and resulted in the world's largest confiscated amount of P-2-P that year: 4,680 l were seized in Gdynia harbour. The Central Bureau of Investigation of the General Police Headquarters in Warsaw conducted the investigation and intelligence proceedings in cooperation with the Belgian police. The case involved an international criminal group specializing in facilitating illegal immigration, trafficking in human beings and money-laundering, as well as drug trafficking. The activities of the group took place in the territories of Belgium, Germany, the Netherlands, Poland and Sweden;

(f) On 29 March 2004, in Shanghai harbour, a container was loaded onto a trans-oceanic freight vessel. According to customs documentation, the container was carrying sesame oil destined for a company specifically set up by an organized criminal group and owned by a person involved in criminal activity. On 30 April 2004, the container, supposedly containing 15,600 l of sesame oil (in 260 60-litre barrels) arrived in Gdynia harbour. On 5 May 2004, officers of the Central Bureau of Investigation and customs officers confiscated the delivery. Following preliminary tests on selected barrels, the substance was identified as P-2-P. Subsequently, the entire consignment was analysed to confirm that P-2-P had been smuggled in 78 60-litre barrels. The total amount of precursor, 4,680 l, would have been sufficient to manufacture approximately 3,300 kilograms of amphetamine using the Leuckart method;

(g) After the detention of the persons responsible for organizing delivery in Belgium and Poland, direct cooperation with INCB was initiated in order to carry out a so-called backtracking investigation. At the same time, direct collaboration with the relevant authorities in China was initiated, leading to the arrest of the detained persons, for diversion of P-2-P from the licit market.

Licit manufacture of 1-phenyl-2-propanone and routes of diversion

According to INCB, 27 cases of diversion and attempted diversion of P-2-P from the licit market were reported between 1995 and 2001. Most of them occurred in India, followed by Germany, Belgium and China. The destination countries

identified included Belgium, Bulgaria, Germany, Hungary, the Netherlands, Romania, Ukraine and the countries that once were part of the former Yugoslavia.

In order to mislead law enforcement authorities, criminals often organize illicit shipments via countries not normally associated with illicit drug production. Quantities of P-2-P smuggled in a single consignment range from a few kilograms or litres to several tons. As regards the modus operandi, there have been instances in which criminal organizations used names of existing companies that were completely unaware that they were named as end-recipients in the customs documents or letters of conveyance. In the majority of cases, however, criminals employed the names of companies regularly importing goods from the countries producing P-2-P, and the goods declared in the customs documents were consistent with the companies' business profiles. Obviously, there have also been instances in which discrepancies between the goods for delivery and a company's profile were spotted, such as when a construction company supposedly imported peaches, and the peaches had in fact been replaced by P-2-P.

Usually, the methods used for the diversion of P-2-P are similar to those observed for other controlled substances:

(a) Attempts by criminal organizations to purchase P-2-P by using forged import licences obtained in the name of companies specifically set up for that purpose ("pillars");

(b) Falsifying customs documentation (declaring fake goods);

(c) Smuggling.

In 13 out of the 27 cases reported to INCB between 1995 and 2001, criminals designed complicated transport routes leading through three or more countries in order to make the verification of the legal status of the consignment more difficult. In six cases, orders were placed in the name of fake companies set up specifically for that purpose ("pillars"), and in two cases false import licences were presented.

It should be emphasized that precursors used for the manufacture of synthetic drugs in Europe are procured mainly on the illicit market, through either smuggling or illicit manufacture. Case studies of attempts at smuggling P-2-P during the past 15 years have highlighted several common features of this category of crime:

(a) In more than 90 per cent of smuggling attempts, the countries of destination were in Europe;

(b) In the majority of cases analysed, the P-2-P was intended to be used as a precursor for the illicit manufacture of amphetamine; only in the United States was it also used for methamphetamine synthesis (some attempts to manufacture methamphetamine from P-2-P in Asia are known as well);

(c) As regards the largest consignments analysed, diversions or illicit manufacture occurred in China, the shipments were dispatched by sea and the destination countries were in Europe;

(d) In recent years, there have been more and more reports of smaller consignments of P-2-P being transported overland across the eastern border of member States of the European Union (that is, from Belarus, the Russian Federation and Ukraine). However, the role of those countries in P-2-P trafficking is not yet known; it has not been determined whether P-2-P is licitly manufactured in those countries and diverted from legitimate trade or whether those countries are merely used as transit countries.*

These trends are also reflected in the fact that more than three quarters of amphetamine seizures worldwide take place in Europe, and two thirds of those take place in Western European countries (Germany, the Netherlands, Sweden, the United Kingdom of Great Britain and Northern Ireland) [3].

Utilization of results of 1-phenyl-2-propanone impurity profiling in police intelligence work

Combining and complementing police intelligence work with information from forensic laboratories dealing with the examination of drugs contribute to building the most desirable system in support of the process of effective suppression of drug-related crime. Several countries and international organizations have joined efforts to enhance this partnership by undertaking various international activities aimed at counteracting cross-border drug-related crime. One of them is Project Prism, launched by INCB in 2002. Its objectives include the strengthening and improvement of cross-border cooperation between law enforcement authorities through the use of specifically tailored, modern strategies and intelligence tools for suppressing the illicit manufacture, smuggling and diversion of precursors.

Project Prism targets five fundamental precursors used in the illicit manufacture of amphetamine-type stimulants, a group of amphetamine derivatives that includes methamphetamine and 3,4-methylenedioxymethamphetamine (MDMA, commonly known as Ecstasy). The precursors of amphetamine-type stimulants are:

(a) Ephedrine and pseudoephedrine, used in the manufacture of methamphetamine;

(b) P-2-P, the main precursor used for the manufacture of amphetamine;

*However, on the basis of numerous instances of reported smuggling of P-2-P into Poland from Belarus and Ukraine, revealed by the Polish investigative services in cooperation with their counterparts in other countries, and from intelligence, it can be concluded that P-2-P is very likely to be licitly manufactured in the Russian Federation and Ukraine and then diverted to illicit markets and then exported. That hypothesis is supported by the analysis of illicit amphetamine manufacture in Poland. Data on the number and types of clandestine laboratories detected and closed down in Poland during the past 10 years show that in the mid-1990s many more laboratories manufactured P-2-P and not amphetamine. The situation has changed recently. For example, in 2000, only 2 out of 14 clandestine laboratories that were shut down specialized in P-2-P manufacture; and in 2004, the figure was only 2 out of 20. Investigations have shown that the reason for the decrease in illicit P-2-P manufacture in Poland was the easy availability of less costly P-2-P, possibly illegally exported from the manufacturing country, Ukraine.

(c) 3,4-methylenedioxyphenyl-2-propane (3,4-MDP-2P) also known as piperonyl methyl ketone (PMK), and safrole used for the manufacture of MDMA (Ecstasy).

Project Prism is based on two parallel approaches:

(a) Tackling the diversion of precursors from licit markets;

(b) Investigative measures aimed at launching backtracking investigations to identify:

(i) Means, methods and routes of diversion, attempted diversion or smuggling;

(ii) Sources and precursor trafficking networks;

(iii) Equipment used in illicit manufacture.

The main aims of investigations in drug-related crime are to identify persons who act as key coordinators of criminal activities and to provide support for future investigations and prevention efforts. Therefore, in the context of backtracking investigations, seizures of illicit precursor consignments should be considered the beginning of the investigative process rather than its conclusion.

A number of regional and international organizations such as INCB, OLAF, the European Police Office (Europol) and the Customs Cooperation Council (also called the World Customs Organization), emphasize the immense importance of providing support for those investigations by means of fast and reliable exchanges of information on licit markets for chemicals, seizures of precursor consignments and results of requested forensic examinations, known as precursor profiling studies.

In order to comply with those requirements in the light of illicit manufacture of synthetic drugs, particularly amphetamine, in Poland the authorities investigating drug-related cases and the forensic services responsible for specialized examinations have been operating in close partnership for several years. A significant outcome of that partnership is Poland's participation in the Eastern Baltic Sea Amphetamine Project, implemented by the Task Force on Organized Crime in the Baltic Sea Region. Thanks to the multilevel cooperation of law enforcement authorities with forensic laboratories in participating countries,* intelligence-led investigations resulted in the identification of several clandestine amphetamine laboratories.

Contribution of impurity profiling of 1-phenyl-2-propanone to law enforcement investigations

In order to propagate and make the best use of the experiences in regional cooperation, the Central Forensic Laboratory of the Police in Poland has proposed

*Cooperation comprises the setting up of computerized forensic and intelligence databanks, exchange of information, the submission of samples of amphetamine seized by all countries participating in the project, comparing amphetamine profiles and their exchange between, for example, the National Forensic Institute in Sweden and the Central Forensic Laboratory of the Police in Poland.

the launching of another profiling project. The subject of the new undertaking is the profiling of P-2-P samples seized, for example, in clandestine laboratories on the territories of participating countries.

The impurity profiling of seized P-2-P samples is aimed at identifying common features of and discrepancies between those samples in order to address the following questions:

(a) Are two or more evidential samples linked with each other?

(b) If links exist, are they of significance, for example, to help to trace a P-2-P sample back to a dealer or a producer?

(c) Can linked samples be traced back to the same local, regional or international network of illicit retailing and distribution?

(d) What is the source of a P-2-P sample (licit or illicit manufacture)?

Data to answer the above questions can be obtained from chemical analyses. They will be of help in the investigative process and may guide further intelligence work by, for example:

(a) Providing information on methods of P-2-P synthesis;

(b) Classifying a sample as part of a group of samples that can be traced back to one source;

(c) Providing supportive evidence on the structure of national, regional and international networks of retailing and distribution;

(d) Determining whether P-2-P samples are from licit or illicit manufacture;

(e) Identifying in a timely manner newly emerging sources of P-2-P.

At the moment, the project is in the implementation phase. Its framework was presented in June 2005 during a meeting of the Expert Group on Narcotics of the Task Force on Organized Crime in the Baltic Sea Region. The project was received with general approval by representatives of all 10 participating countries. Lithuania and Sweden have already expressed their intention to participate, and the decisions of other countries are expected soon.

Also in 2005, representatives of the Polish Police held an official meeting with representatives of the Ukrainian militia to discuss partnership in the area of combating international drug-related crime. On that occasion, the Polish representation presented the P-2-P profiling project and appealed to the Ukrainian militia to support the project by contributing data on the licit market of P-2-P in Ukraine (e.g. the number of manufacturers, the total production volume). Another important issue was the provision of samples from all companies licitly manufacturing P-2-P, to be used as authenticated reference samples in comparative analyses.

Forensic examination of 1-phenyl-2-propanone

From an analytical point of view, the identification of P-2-P is very straightforward and does not pose any problems. The best and quickest results are

obtained by means of gas chromatography/mass spectrometry (GC/MS), by which P-2-P can be identified on the basis of two parameters: retention time and mass spectrum (see figure I). For investigative purposes, in addition to identifying P-2-P, linking samples with a source or a given synthesis batch and identifying the synthesis route are important issues. In order to address those points, the following multi-stage methodology of P-2-P impurity profiling has been elaborated in the Central Forensic Laboratory of the Police:

(a) Sample preparation;

(b) Analysis of samples by means of GC/MS;

(c) Identification of impurities;

(d) Statistical analysis of results;

(e) Introducing the results into the database.

Analytical procedure

Preparation of 1-phenyl-2-propanone samples for analysis

The methodology of P-2-P impurity profiling was elaborated using 80 samples from seized consignments, which investigative information showed to have been produced by different synthesis routes. Every sample was prepared for analysis by mixing 100 ml of P-2-P and 1 ml of chloroform with an internal standard (diphenylamine at a concentration of 0.3 mg/ml); 1 ml of that solution was used for analysis. A typical impurity profile of P-2-P is presented in figure VIII.

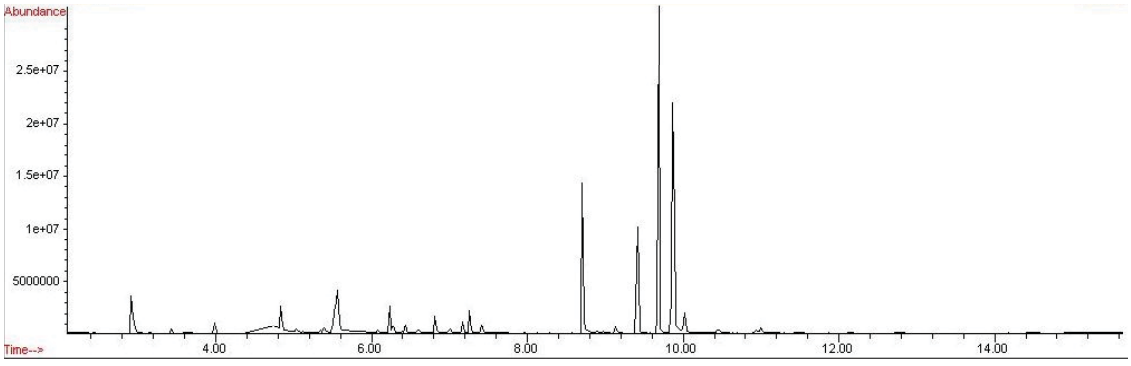
Parameters of analysis by gas chromatography/mass spectrometry

Operation conditions

Instrument:	GC HP-6890/MSD HP 5973 (Hewlett Packard)
Column:	HP5 MS 30 m x 250 μm x 0.25 μm capillary column
Carrier gas:	helium, continuous flow at 1.6 ml/min, split: 20:1
Temperature programme:	70 °C for 0.5 min, 70°-290 °C with ramp of 15 °C/min, 290 °C for 0.5 min (total analysis time: 15.67 min)
Transfer line temperature:	290 °C
Detector:	MSD (TIC 40.5-550 amu), detector turned off in interval from 4.35 to 4.65 min*

*In this process the detector was turned off between 4.35 and 4.65 min; that is, at the expected retention time of the P-2-P peak. A high concentration of P-2-P in the prepared solution would have caused saturation of the detector and would have interfered with the identification of the remaining peaks in the chromatogram.

Figure VIII. Impurity profile of a 1-phenyl-2-propanone sample, obtained through gas chromatography/mass spectrometry



The repeatability of the method was assessed on the basis of 10 analyses of one randomly selected P-2-P sample. All tests were performed on the same day. The standard deviation and relative standard deviation were calculated for retention times and peak areas of two selected peaks, the internal standard (diphenylamine) and phenylacetic acid. The results obtained are presented in table 1.

Table 1. Analyses of one randomly selected sample of 1-phenyl-2-propanone: retention times and peak areas of diphenylamine and phenylacetic acid

	Diphenylamine		*Phenylacetic acid*	
Parameter	*Retention time (min)*	*Peak area (counts)*	*Retention time (min)*	*Peak area (counts)*
Average	8.7179	207 165 059	5.5688	203 856 669
Standard deviation	0.001853	10 983 337	0.001549	4 653 705.3
Relative standard deviation (percentage)	0.02	5.30	0.03	2.28

The reproducibility of the method was determined in 30 analyses of various randomly selected P-2-P samples. The analyses were performed on different days during one month. Standard deviation and relative standard deviation were calculated for the internal standard (diphenylamine). The results obtained are presented in table 2.

Table 2. Analyses of various randomly selected samples of 1-phenyl-2-propanone: retention times and peak areas of diphenylamine

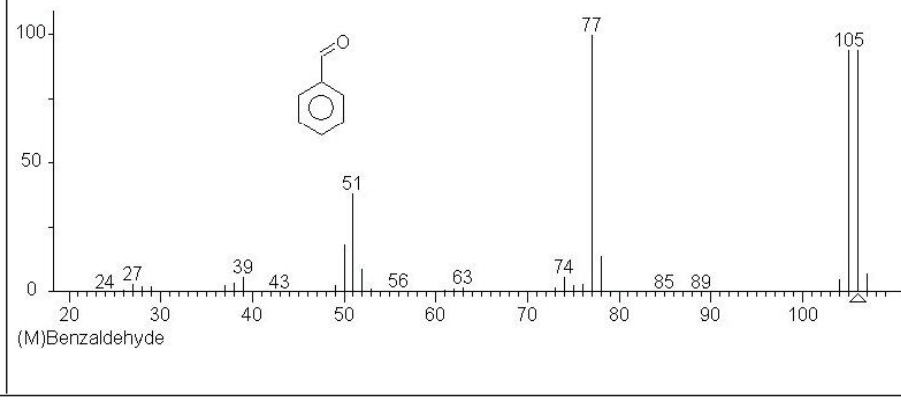
	Diphenylamine	
Parameter	*Retention time (min)*	*Peak area (counts)*
Average	8.717867	224 402 574
Standard deviation	0.001737	21 425 609
Relative standard deviation (percentage)	0.02	9.55

The above findings confirm that the method is repeatable and reproducible.

Identification of impurities

In the 80 P-2-P samples analysed, 36 impurities were identified on the basis of their mass spectra and a comparison of predicted and actual retention time. Fourteen marker impurities were selected for sample comparisons; that is, to make profiles for the entire population of samples (see figure IX).

Figure IX. Impurities identified in samples of 1-phenyl-2-propanone

Retention time (min)	*Name, structural formula, mass spectrum*	*Number of marker*
2.93		

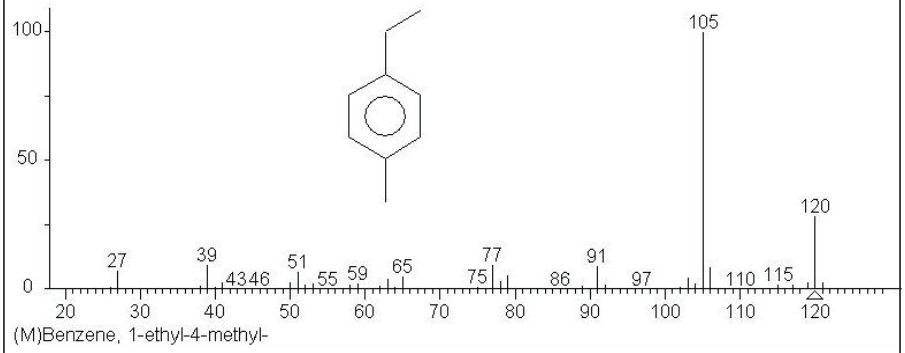
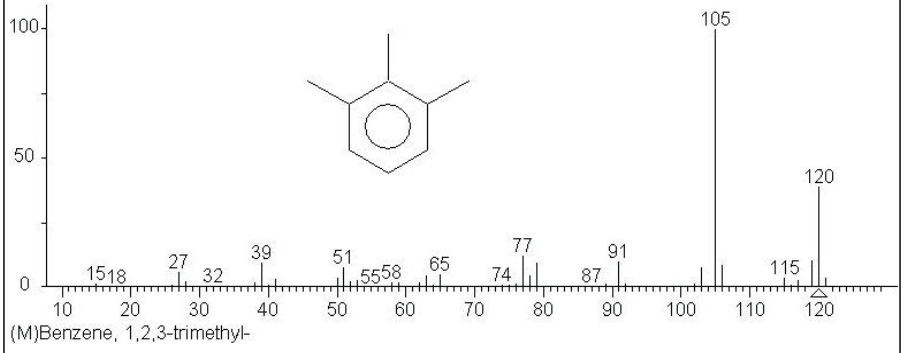
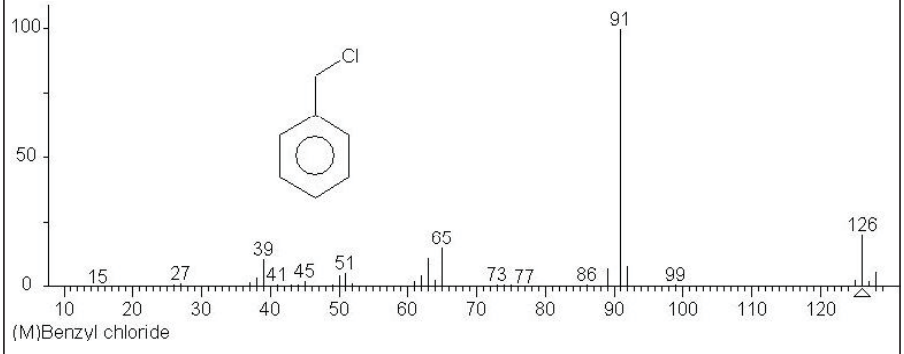
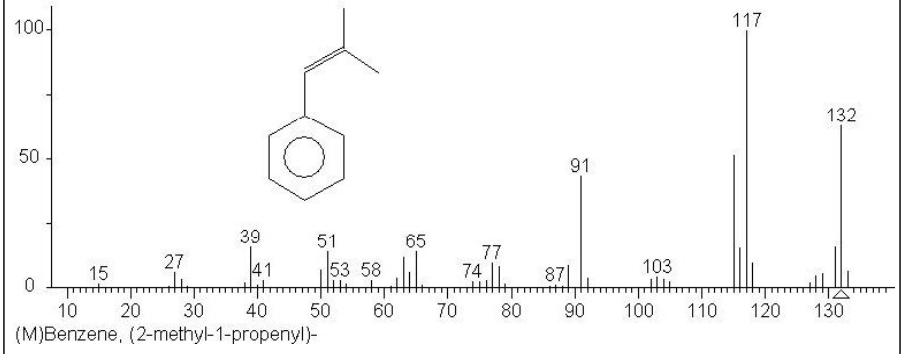
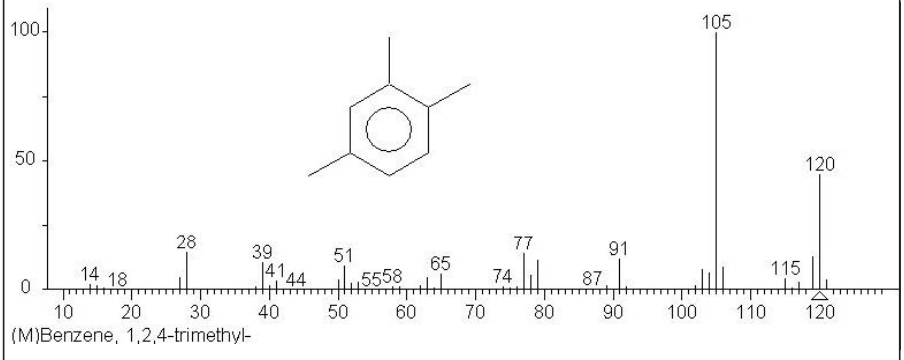
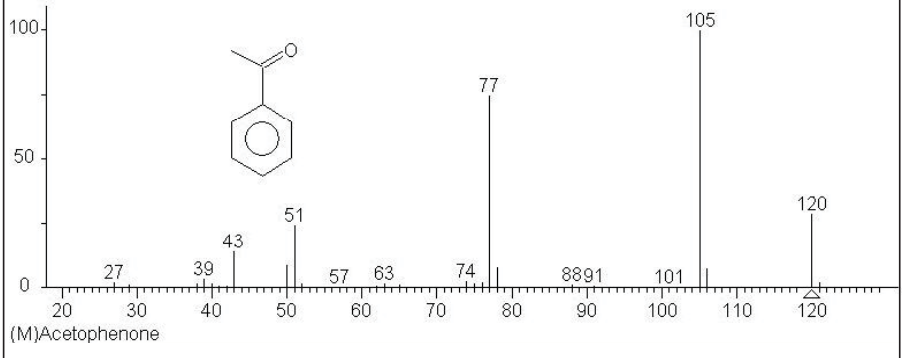
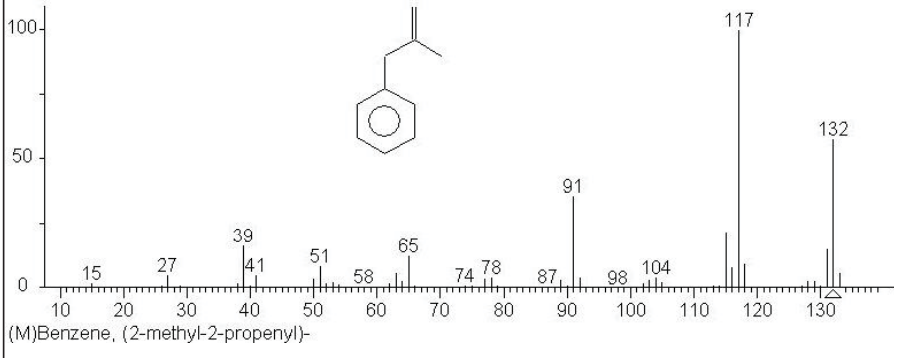
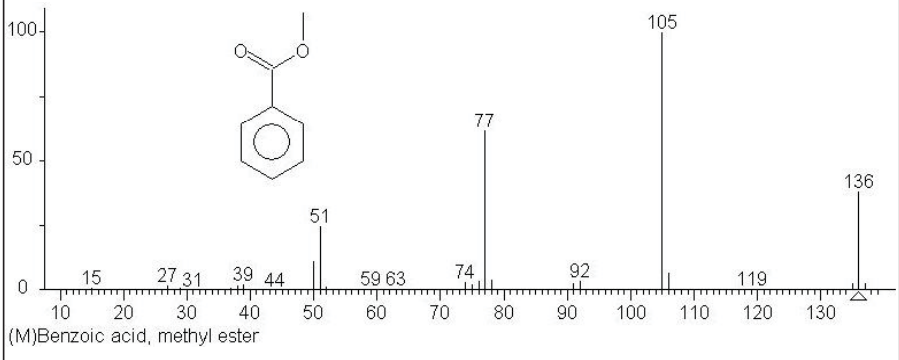
Retention time (min)	*Name, structural formula, mass spectrum*	*Number of marker*
3.08	 (M)Benzene, 1-ethyl-4-methyl-	
3.20	 (M)Benzene, 1,2,3-trimethyl-	
3.38	 (M)Benzyl chloride	
3.44	 (M)Benzene, (2-methyl-1-propenyl)-	1

Figure IX. ***(continued)***

Retention time (min)	*Name, structural formula, mass spectrum*	*Number of marker*
3.46		
3.85		2
4.00		3
4.12		

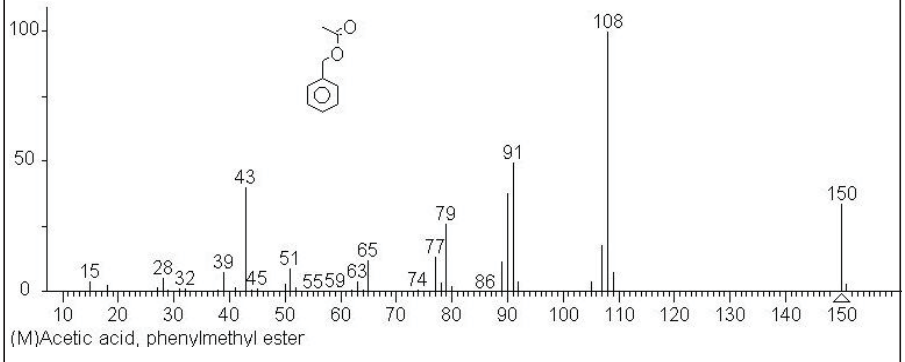
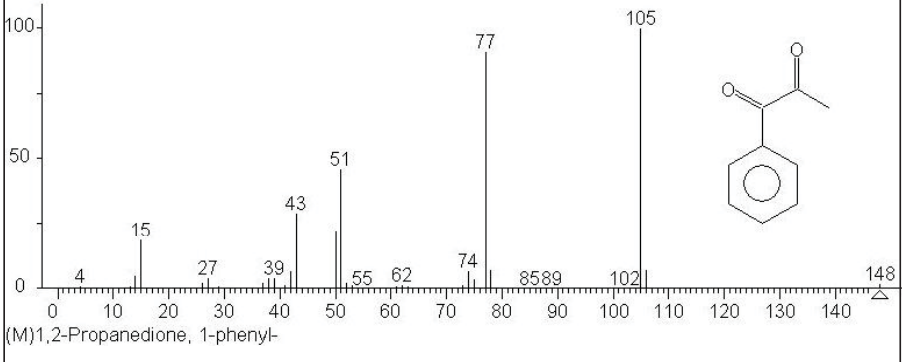
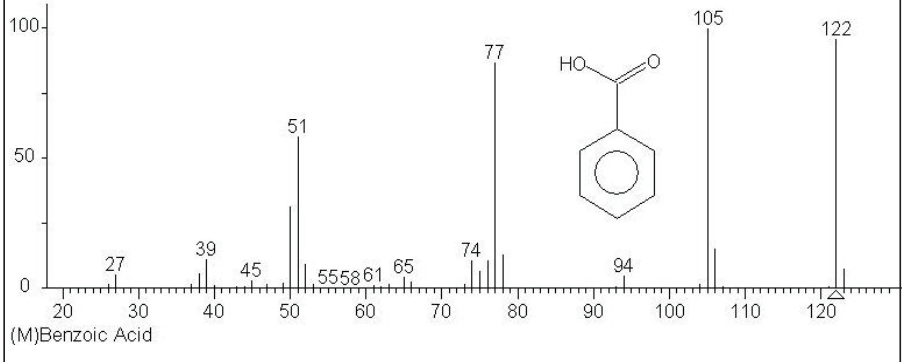
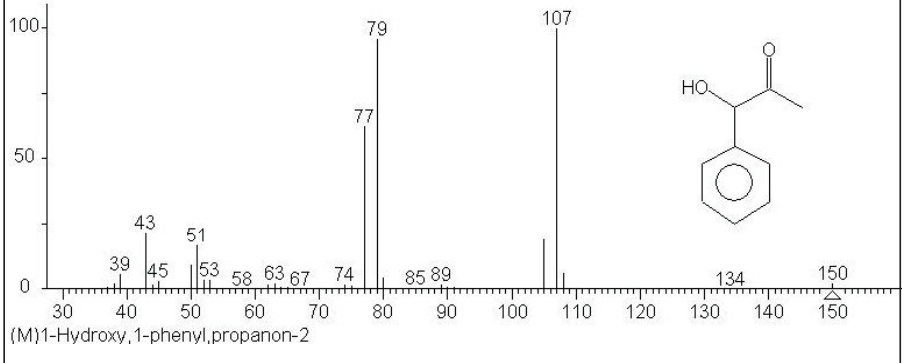
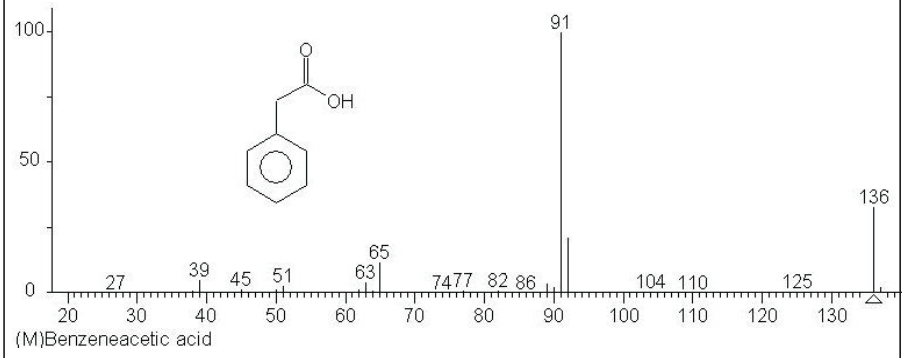
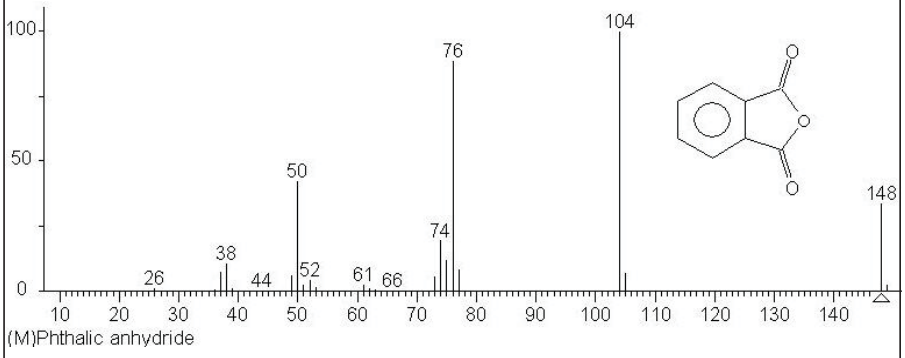
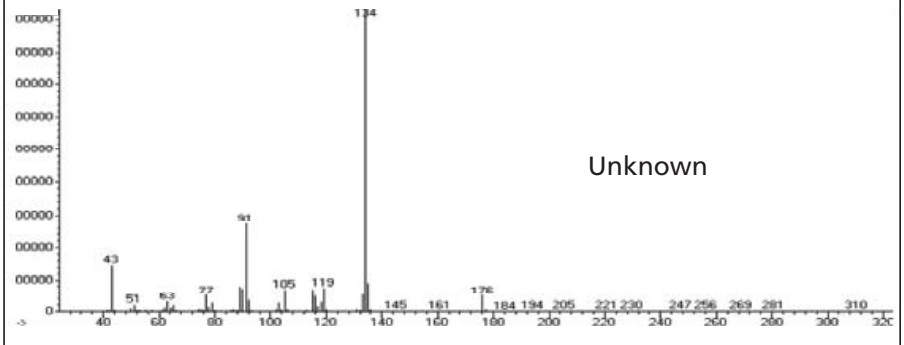
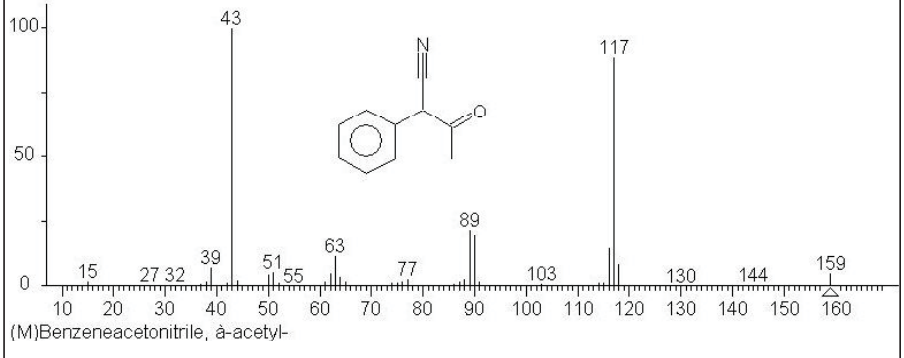
Retention time (min)	*Name, structural formula, mass spectrum*	*Number of marker*
4.77		
4.84		
4.98		4
5.40		5

Figure IX. ***(continued)***

Retention time (min)	*Name, structural formula, mass spectrum*	*Number of marker*
5.57		6
6.18		
6.25	 Unknown	7
6.29		8

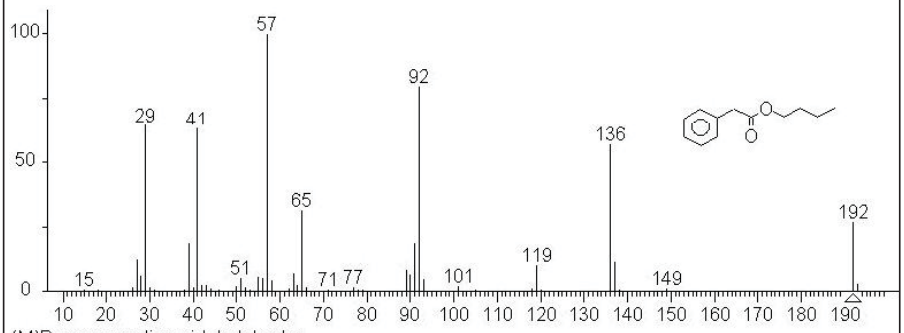
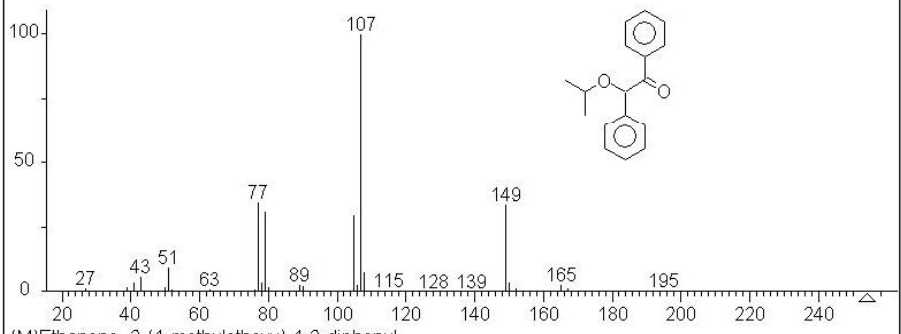
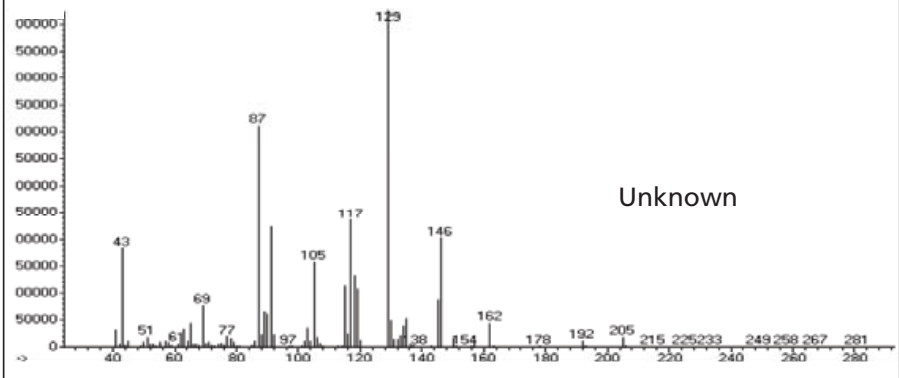
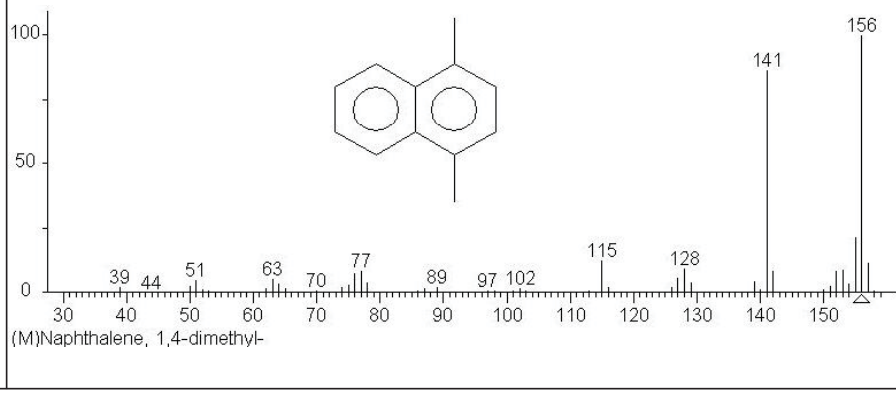
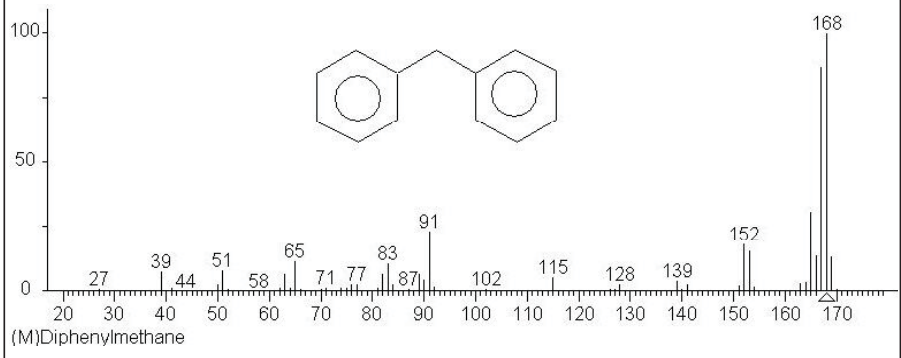
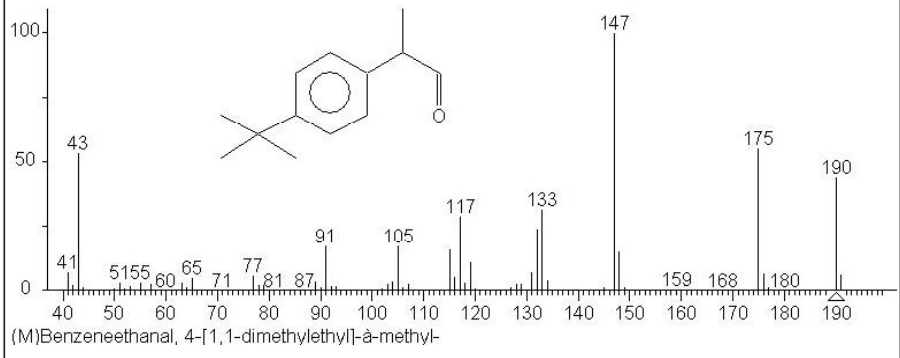
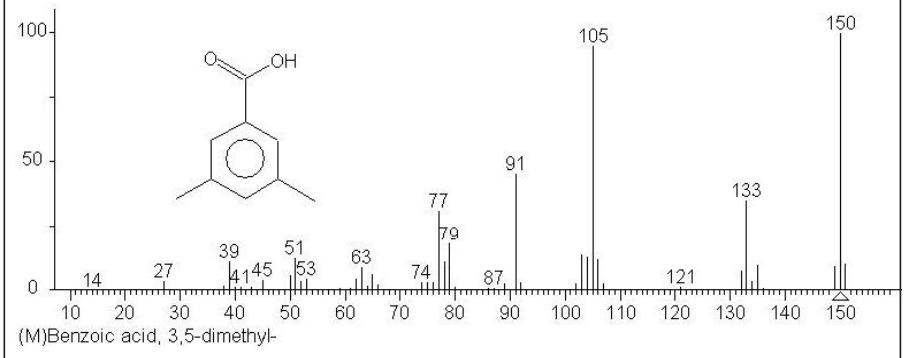
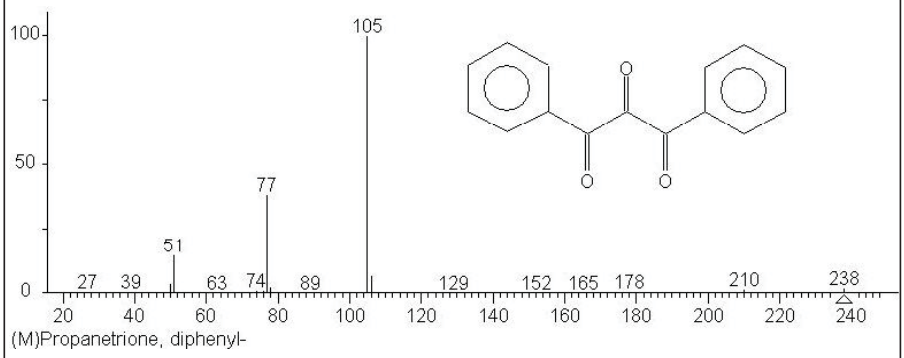
Retention time (min)	*Name, structural formula, mass spectrum*	*Number of marker*
6.80		9
6.87		
7.00	 Unknown	10
7.11		

Figure IX. ***(continued)***

Retention time (min)	*Name, structural formula, mass spectrum*	*Number of marker*
7.20		
7.31		11
7.78		
7.89		

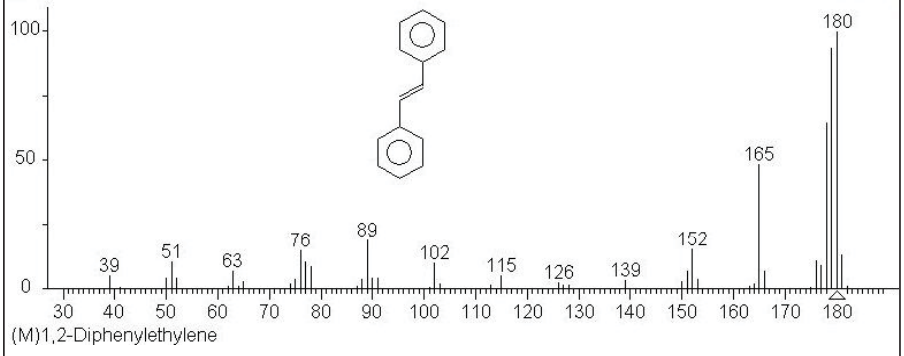
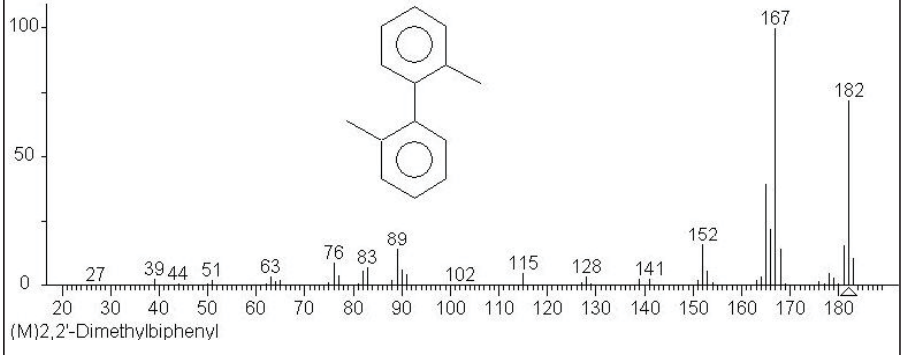
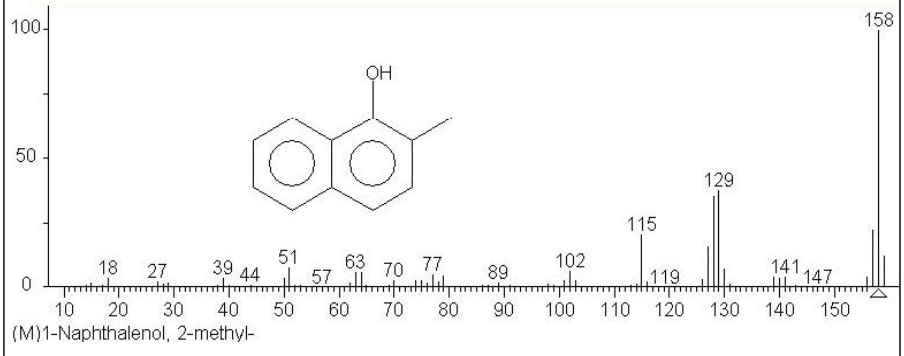
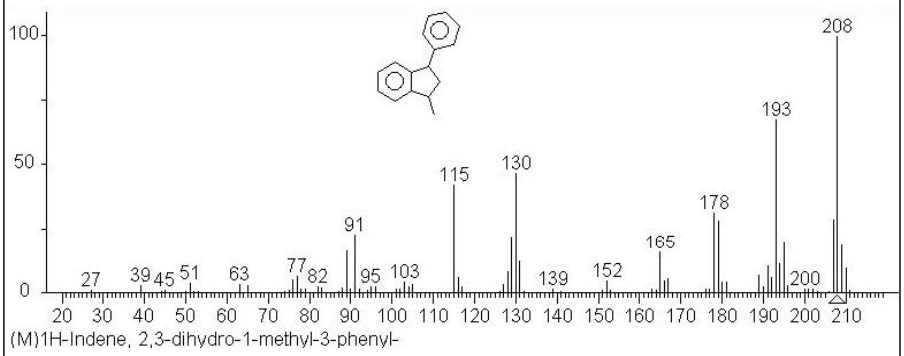
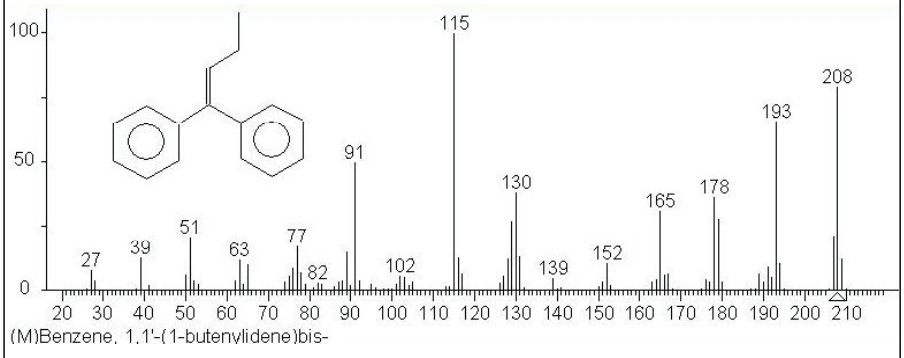
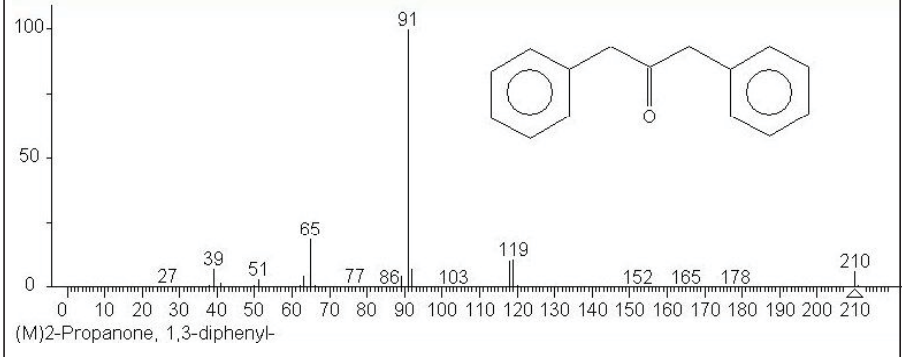
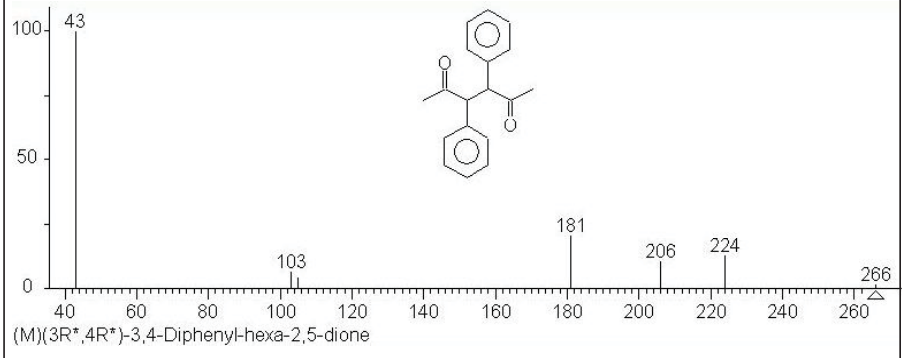
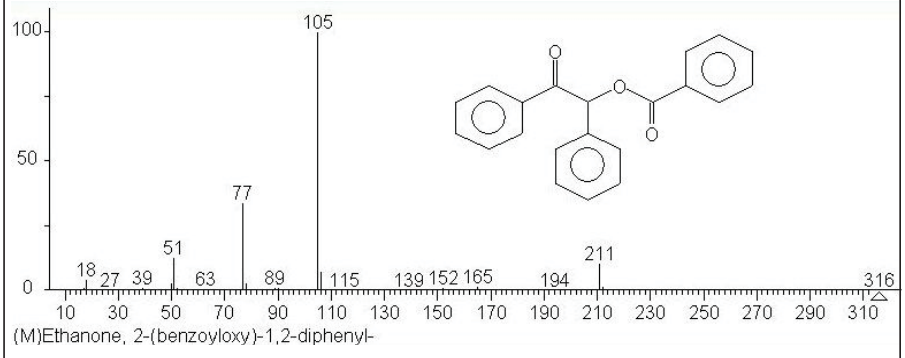
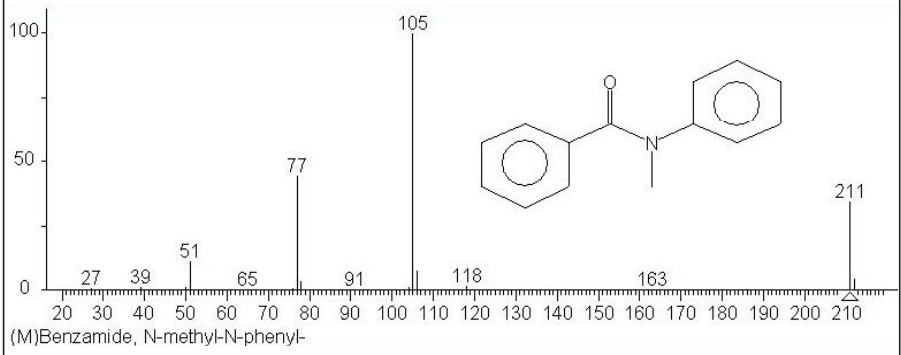
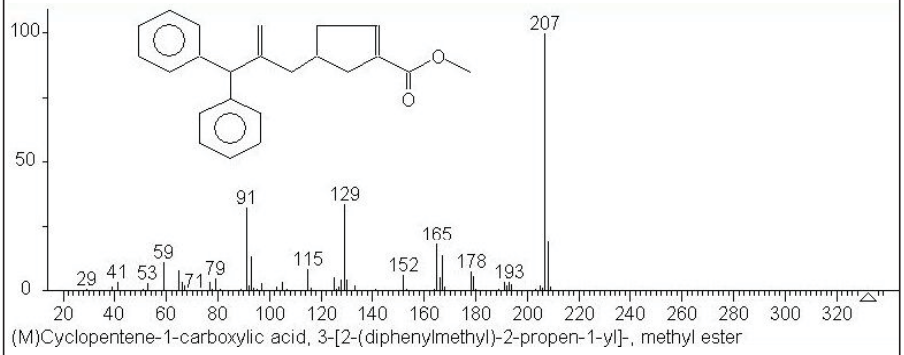
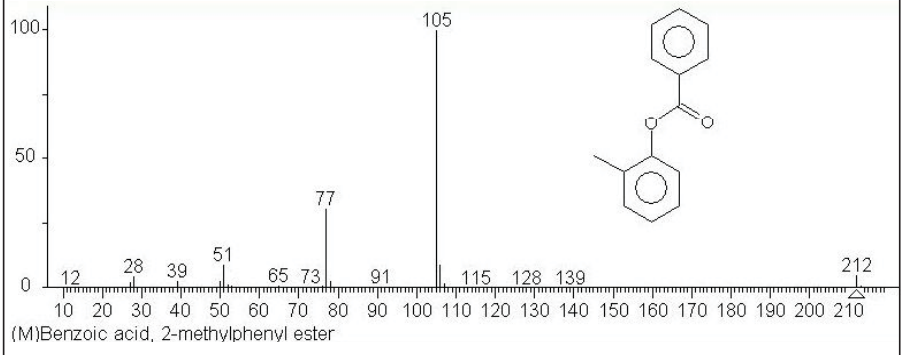
Retention time (min)	*Name, structural formula, mass spectrum*	*Number of marker*
7.95	 (M)1,2-Diphenylethylene	
8.07	 (M)2,2'-Dimethylbiphenyl	
9.14	 (M)1-Naphthalenol, 2-methyl-	
9.42	 (M)1H-Indene, 2,3-dihydro-1-methyl-3-phenyl-	

Figure IX. ***(continued)***

Retention time (min)	*Name, structural formula, mass spectrum*	*Number of marker*
9.69		
9.87		12
10.46		13
11.39		14

Retention time (min)	*Name, structural formula, mass spectrum*	*Number of marker*
11.41		
11.52		
12.23		

Peak areas of the 14 compounds chosen as markers were included in statistical calculations. The selection of the 14 marker impurities was as follows:

(a) Twelve compounds were selected as general markers (numbers 1-5, 7 and 9-14) on the basis of frequency of occurrence in various P-2-P samples analysed. They are independent of the P-2-P synthesis route;

(b) Two markers were selected as route-specific markers, indicative of a given P-2-P synthesis route (number 6 for P-2-P synthesized from phenylacetic acid and number 8 for P-2-P synthesized from benzyl cyanide).

The route-specific marker characteristic for P-2-P synthesized from phenylacetic acid is the remainder of unreacted starting material, phenylacetic acid (marker number 6). By contrast, the impurity found in profiles of P-2-P synthesized from benzyl cyanide is α-phenylacetoacetonitrile (marker number 8), the intermediate product generated in the first stage of synthesis.

In some cases, batches of P-2-P are diluted with acetophenone (marker number 2) to increase the volume (bulk) of the P-2-P precursor. Contamination with that substance thus becomes a characteristic feature, which is why it was included in the profile. From a forensic point of view, it is important to recognize that amphetamine made from P-2-P diluted with acetophenone is characterized by specific impurities. It is therefore possible, on the basis of the impurity profile of the end-product amphetamine, to determine that a mixture of P-2-P and acetophenone was used as the starting material. It is also possible to establish links between amphetamine and the P-2-P samples diluted by acetophenone.

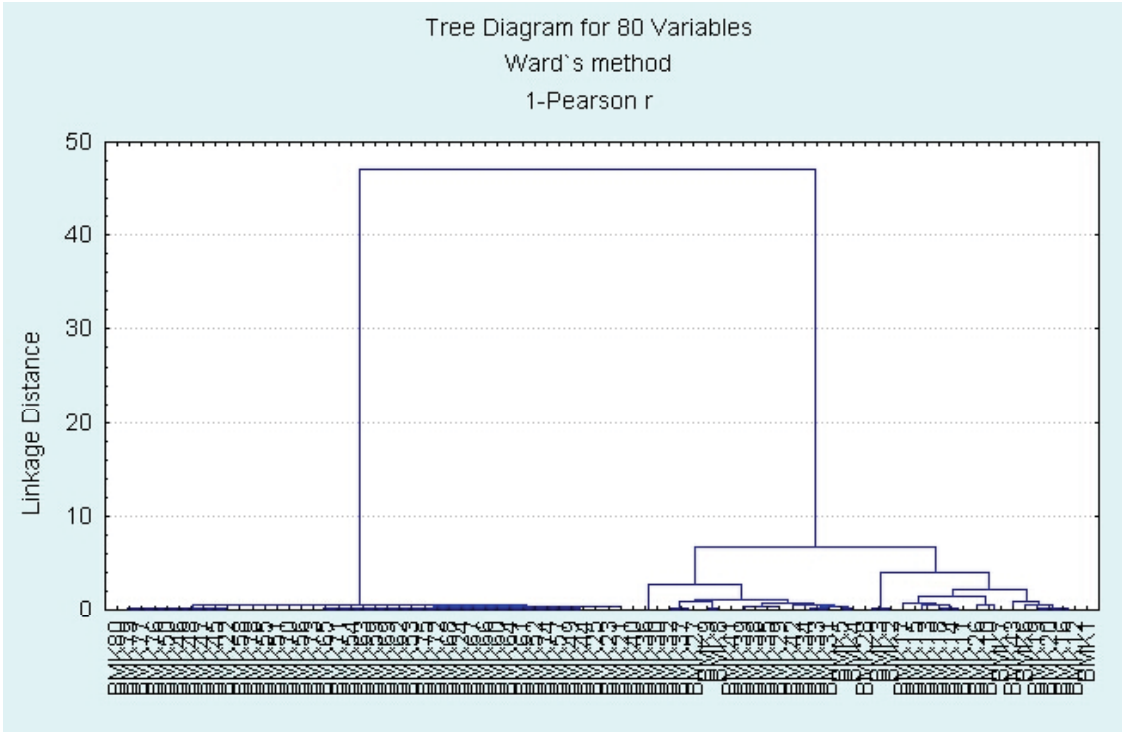
As a result of the impurity analysis, it was possible to classify the 80 P-2-P samples into four groups, characterized by key marker impurities: *(a)* phenylacetic acid group; *(b)* *a*-phenylacetoacetonitrile group; *(c)* acetophenone group; and *(d)* unknown method group, when none of the aforementioned substances was detected. Hence, the selected markers of the P-2-P profiles accurately reflect similarities and discrepancies between individual P-2-P samples.

Statistical analysis of results

A statistical analysis was carried out on the impurity profiles of 80 P-2-P samples from various seizures. A combination of different methods of cluster analyses (complete linkage, single linkage and Ward's methods) and various distance measurements (Euclidean distance, square of Euclidean distance, city-block (Manhattan) distance, Chebychev's distance, 1-Pearson r, power distance, percentage of disagreement) between individual P-2-P samples was applied. Calculations were performed with the peak areas of the 14 selected markers, standardized according to the formula $SV = (V - \mu V)/S_v$, where SV is the standard value, V is the original value, μV is the mean of original values and S_v is the standard deviation of original values.

The application of most of the methods resulted in a division of the 80 samples into three clusters. The separation of the clusters was most pronounced for the combination of 1-Pearson r distance with Ward's method (a method of cluster analysis based on minimalization of the variance in the clusters) (see figure X). The 1-Pearson r distance is defined according to the formula $d_{ik} = [1- r_{ik}^2]^{1/2}$, where d_{ik} is the distance between samples i and k and r_{ik} is the Pearson correlation coefficient between samples i and k. For similar samples the correlation coefficient is close to one and the distance between samples is close to zero.

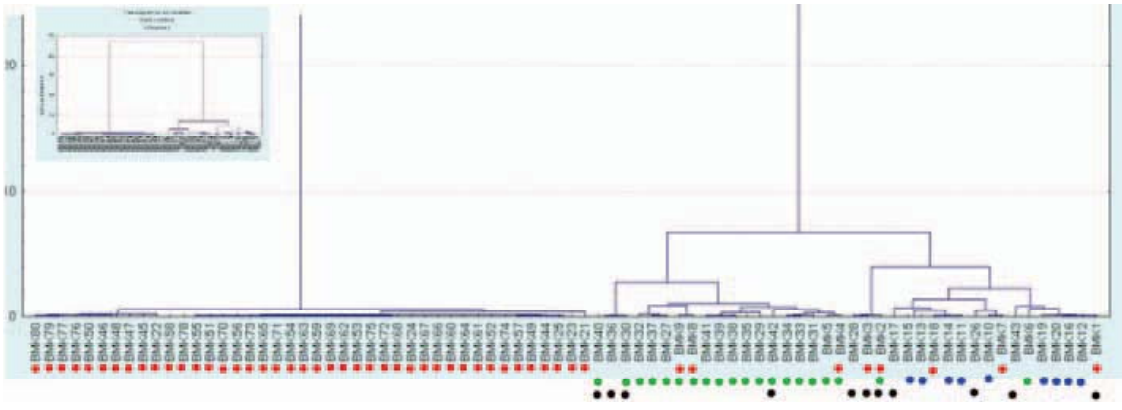
Figure X. Result of cluster analysis of 80 samples of 1-phenyl-2-propanone



Interpretation of statistical data

The P-2-P samples analysed were produced by three synthesis methods: using phenylacetic acid, using benzyl cyanide and by an unknown method. Those three synthesis routes are reflected in three clusters resulting from the cluster analysis (indicated by coloured dots in figure XI).

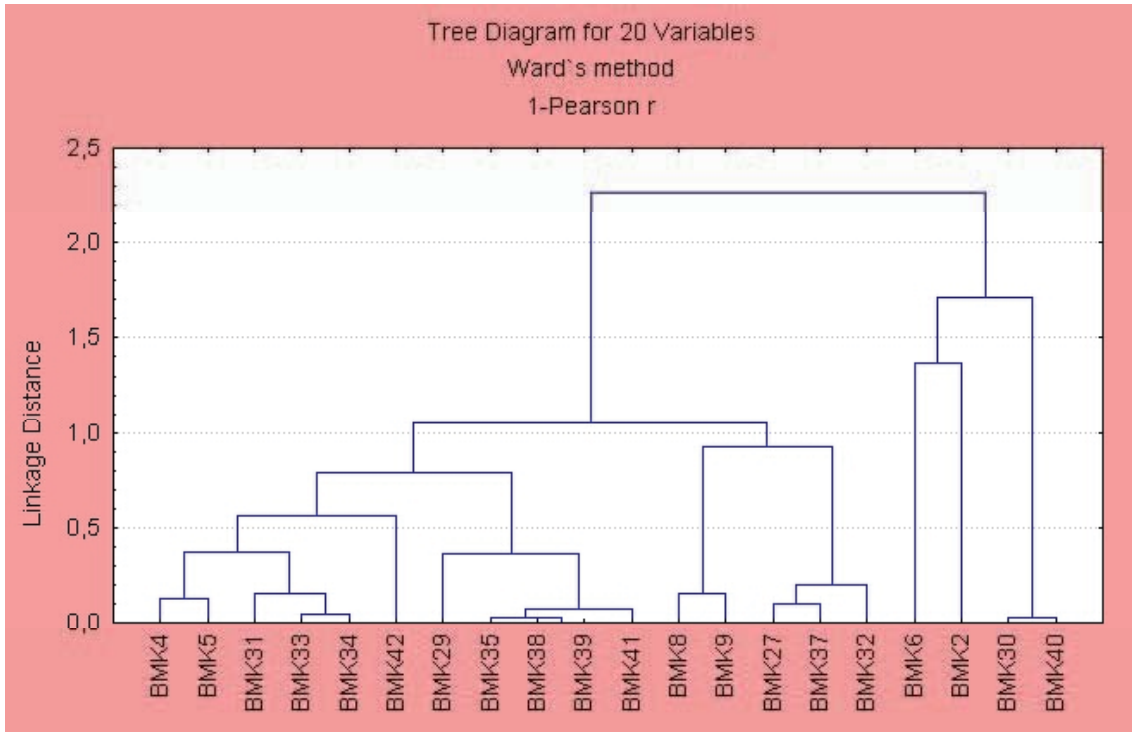
Figure XI. Results of cluster analysis



- P-2-P from phenylacetic acid (red dot)
- P-2-P from benzyl cyanide (green dot)
- P-2-P obtained through unknown method (blue dot)
- P-2-P containing acetophenone (black dot)

Each of the four groups can be further divided into profile classes, or subgroups. Thus, cluster analysis can be used for the differentiation of impurity profiles according to the synthesis method, but also according to batches or sources. For example, the benzyl cyanide group is further split into several clusters (see figure XII).

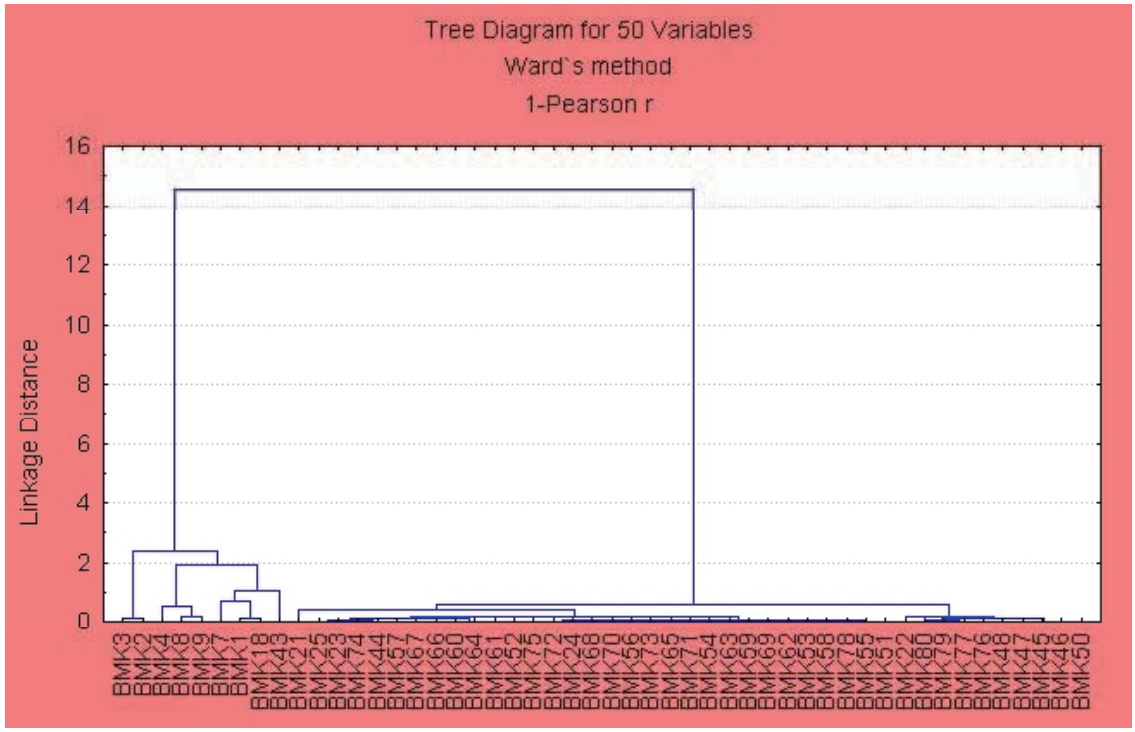
Figure XII. Tree diagram for the benzyl cyanide group



For the phenylacetic acid group, there are several subgroups, indicating differences among samples (see figure XIII). However, the significance of those differences is not yet clear. The objective of further examinations will be to determine the threshold values of the linkage distances classifying P-2-P samples as belonging to the same batch (i.e. same synthesis run) or as coming from the same laboratory but different synthesis runs.

The results of the P-2-P analyses are stored in both a forensic and a police database. The forensic database is maintained by the Central Forensic Laboratory of the Police in Warsaw and comprises P-2-P impurity profiles, results of analytical tests (purity, additives, main impurities), police and laboratory case identification numbers, place and date of seizure, case circumstances, volume of seizure and information on similarities to previously examined P-2-P samples. The police database comprises detailed data on confiscations, such as names, telephone numbers and addresses of persons involved, modus operandi and forensic and law enforcement links to other seizures. In addition, the database

Figure XIII. Tree diagram for the phenylacetic acid group



contains information from the forensic database (on purity, additives, forensic links to other samples) with relevant police case identification numbers that can be used for cross-referencing the databases. The police database is maintained by the Central Bureau of Investigation of the General Police Headquarters.

The databases facilitate the monitoring of the P-2-P market in Poland, the identification of sources of P-2-P (manufactured licitly or illicitly) and the linking of police cases based on the origin of the precursor.

Conclusions

Amphetamine is one of the most popular synthetic drugs in Europe. Its illicit manufacture usually requires the use of the precursor P-2-P. The source of precursor may be licit or illicit manufacture. In Poland, the system of P-2-P profiling elaborated by the Central Forensic Laboratory of the Police enables the determination of the route of synthesis and the identification of samples from the same source. Results of analyses and information on circumstances of seizures are entered into the forensic and police databases, which are used in intelligence and investigative police work.

All aspects discussed above accentuate the crucial importance of the interaction of police investigative and intelligence services with the forensic sector in the process of effective detection and suppression of drug-related crime.

References

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